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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,794	09/01/2000	Meir S. Sacks	286262-00005	5973

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ALAN G. TOWNER
PIETRAGALLO, BOSICK & GORDON
ONE OXFORD CENTRE
301 GRANT STREET 38TH FLOOR
Pittsburgh, PA 15219

EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/653,794

Applicant(s)

SACKS ET AL.

Examiner

Gollamudi S Kishore, Ph.D

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13, 18, 19 and 21-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13, 18-19 and 21-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

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DETAILED ACTION

The amendment dated 7-30-04 is acknowledged.

Claims included in the prosecution are 13, 18-19 and 21-25.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 13, 18-19 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel (6,207,713) or Wallace (6,476,037 view of Chobanian et al (6,139,847) of record.

Fossel discloses topical delivery of L-arginine (nitric oxide inducer and vasodilator) or the treatment of erectile dysfunction (note abstract, Example 3 and claims).

Similarly, Wallace discloses the topical administration of L-arginine for the treatment of erectile dysfunction (abstract, col. 15, line 53 et seq., Examples and claims).

Chobanian et al while disclosing a treatment of fibrosis teach that antioxidants such as ascorbate, tocopherol and beta-carotene are NO catabolism inhibitors and

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advocates the use of the combination of NO stimulators (L-arginine) and NO catabolism inhibitors (note the abstract, col. 3, line 6 through col. 4, line 67, col. 5, line 40, Example 1 and claims). Chobanian further teaches the knowledge in the art of the use of NO donors for the treatment of conditions including impotence (col. 3, lines 6-10).

The inclusion of an antioxidant in the L-arginine containing compositions of Fossel or Wallace for the treatment of erectile dysfunction would have been obvious to one of ordinary skill in the art, with the expectation of obtaining at least an additive effect, since Chobanian teaches that antioxidants are NO catabolism inhibitors and that they could be used in combination with NO stimulators. Although neither Fossel nor Wallace teach the use of the composition for female sexual dysfunction by topical application to the clitoris, it would have been obvious to one of ordinary skill in the art to use the composition for females with a reasonable expectation of success since clitoris is supplied with blood vessels and the principle of vasodilatation is the same.

5. Claims 13, 18-19 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel or Wallace in view of Chobanian et al as set forth above, further in view of Duckett et al (6007,824) by itself or in further combination with Wyson (6,031,002)

The teachings of Fossel, Wallace and Chobanian have been discussed above. As pointed out above, what are lacking in Fossel, Wallace and Chobanian are the teachings of the applicability of the arginine derivatives for the treatment of female sexual dysfunction.

Duckett et al as discussed before, disclose compositions containing L-arginine and ginseng (antioxidant) for the treatment female sexual dysfunction. Duckett et al teach that the sexual stimulation causes local release of NO resulting in the smooth

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muscle relaxation and the increased blood flow. They further teach that L-arginine releases NO resulting in smooth muscle relaxation and increased inflow of blood (note the abstract, col. 1, line 12 through col. 2, line 46, col. 3, line 65 through col. 4, line 50 and claims). The mode of administration in Duckett however, is oral and not topical.

Wysor as discussed before, while disclosing prostaglandin (vasodilator) formulations for enhancing female sexual response teaches that the formulations can be applied topically to the genitals and such a topical treatment is highly effective. Wysor further teaches the use of liposome formulations for the delivery of the composition (note the abstract, columns 1-3 and claims).

In essence, the reference of Duckett shows that the principle of NO release and the increased blood flow in females by the vasodilator, arginine and that of Wysor shows that a vasodilator can be applied topically the genitals to treat female sexual dysfunction.

One of ordinary skill in the art would be motivated further to use the composition of arginine and the antioxidants of Fossel, Wallace and Chobanian to treat the female dysfunction since the effectiveness of arginine against female dysfunction and that of Wysor shows that a vasodilator composition can be applied topically to the female genitals to achieve the desired goal.

6. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fossel, Wallace in view of Chobanian et al (6,139,847) as set forth above, OR Fossel, Wallace in view of Chobanian et al (6,139,847) further in view of Duckett et al (6007,824) by itself or in combination with Wyson (6,031,002) as set forth above, further in view of Quan (6,180,133).

The teaching of Fossel, Wallace, Chobanian, Duckett, and Wysor has been discussed above. What is lacking in these references is the use of ascorbyl palmitate.

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Quan while disclosing topical antioxidant formulations teaches that ascorbyl palmitate is stable and due to its fat solubility, it penetrates the skin more readily than ascorbic acid reaching comparatively high levels in much shorter periods of time (note col. 5, lines 45-55).

The use of ascorbyl palmitate or ascorbyl palmitate in combination with ascorbic acid would have been obvious to one of ordinary skill in the art since ester form is fat soluble and penetrates the skin more readily as taught by Quan. The use of a mixture would have been obvious since such a use would achieve both rapid slow response times.

Applicant's arguments based on the declaration submitted by Dr. Sacks have been fully considered, but are not found to be persuasive. The allowability of the claims will be considered once applicant addresses the following issues. First of all, it is unclear whether the same 5 women were applied with control, then arginine plus antioxidant and then with an ethyl ester of L-arginine and antioxidant or there were 5 women in each group. Secondly, the examiner is unable to determine the significance of the results since 1) so statistical evaluation was done; 2) no data regarding the age and the menstrual cycle time are provided since these determine the sexual responses by women; 3) there are no controls using L-arginine or ethyl ester of arginine or the antioxidants by themselves. Such an evaluation is essential since both arginine and the antioxidants by themselves have some effect on sexual activity as evident from the above cited references. Surprisingly, applicant finds no response at all for a combination of L-arginine and antioxidant in 5 women tested. If that were to be the case, how can one be sure that any antioxidant would work well with even the ethyl ester of arginine?

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Finally, it should be pointed out the experiments appear to have been conducted with a 1:1 combination of ascorbic acid and ascorbyl palmitate (and in 1:2 ratio with arginine or arginine ester), where as the claims are drawn to 'an effective amount of an antioxidant'.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, Ph.D
Primary Examiner
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GSK